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Does atypical interoception following physical change contribute to sex differences in mental illness?

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Abstract

Sex differences in the prevalence and presentation of mental illnesses are well-documented. Women are more likely to experience common mental health disorders (e.g. anxiety and depression), and when they experience these conditions they often present differently to men (e.g., women are more likely to report somatic complaints). Periods of physical and hormonal change (e.g., adolescence, pregnancy and menopause) are particular risk periods for the development of mental illness in women. In this paper, we advance the proposal that interoception (the perception of the body's internal state) is one mechanism that might explain sex differences in vulnerability to mental illness. We argue that known sex differences in interoception, whereby women, compared to men, report heightened attention to internal signals coupled with worse interoceptive accuracy, may result from the increased amount of physical and hormonal change women experience across development. Given links between interoception and mental health, we propose that sex differences in interoception may partly explain sex differences in the prevalence and presentation of certain mental illnesses. Further scrutiny of this proposal may aid our understanding of sex differences in mental illness with implications for assessment, early intervention and the development of novel treatment approaches.

Key words: Interoception; Mental illness; Sex differences; Gender differences; Adolescence; Pregnancy; Menopause

Mental illness significantly contributes towards the global burden of disease (Whiteford et al., 2015). Across most of development many common mental disorders (CMDs; e.g., anxiety and depression) are more prevalent in women than men (Kessler et al., 1993; Whiteford et al., 2015), with sex differences in symptom profiles also apparent; for example, women with depression are more likely to report somatic symptoms than men (Marcus et al., 2008). Whilst sex differences in mental illnesses are well-documented, the source(s) of these differences are not fully understood. In women, mental illness often manifests during transitional periods (periods of substantial physical, social and personal change) such as adolescence, pregnancy, and menopause (Altemus et al., 2014). Whether a common mechanism contributes towards mental illness during these risk periods, which can elucidate sex differences in CMDs, remains an open question.

Interoception, the perception of the body's internal state (Khalsa et al., 2018), is one plausible mechanism that may contribute to individual differences in vulnerability to mental illness. Interoception has been found to affect fundamental cognitive domains, impairments in which have previously been identified as risk factors for poor mental health (e.g., social cognition, emotion regulation, sense-of-self, reward learning, and decision-making; Khalsa et al., 2018). Atypical interoception (abnormally accurate, inaccurate or poor metacognitive insight) is also observed across multiple mental health conditions, where it is thought to contribute towards several transdiagnostic (e.g. low mood, elevated anxiety) and disorder-specific symptoms (e.g. addiction cravings, atypical eating in eating disorders; Khalsa et al., 2018; Khalsa and Lapidus, 2016).

Sex differences in interoception are often reported in typical and/or community samples. In comparison to men, women exhibit poorer objective interoceptive accuracy (e.g. cardiac, respiratory, gastric and sexual arousal; Grabauskaitė et al., 2017; Suschinsky and

Lalumière, 2012; Harver et al., 1993; Whitehead and Drescher, 1980), even after physiological differences (e.g., blood pressure, body mass index, heart rate variability and resting heart rate) have been accounted for (Murphy et al., 2018), and are more likely to rely on external cues for gauging internal states (Pennebaker and Roberts, 1992). Furthermore, women generally report increased attention to internal sensations and more somatic (interoceptive) complaints (e.g., Grabauskaitė et al., 2017; Barsky et al., 2001). These sex differences raise the possibility that, on an individual level, women may be more likely to exhibit a pattern of interoceptive processing characterised by heightened interoceptive attention and poor objective accuracy (referred to as high ‘trait interoceptive prediction error’; TIPE). Importantly, high TIPE has been linked to elevated anxiety (Garfinkel et al., 2016). If, as the evidence suggests, high TIPE is more common in women, it is therefore possible that high TIPE may partly explain why anxiety disorders are more common in women than men (Whiteford et al., 2015).

Although frequently reported, the causes of sex differences in interoception are unclear. Research on somatic symptom reporting suggests that several factors (biological and social) may contribute towards women’s heightened attention to physical sensations and increased pain sensitivity. For example, sex differences in physiology (e.g., peripheral afferent pathways, hormones), experiences (e.g., physical change, socialisation) and willingness to report have all been proposed to contribute towards increased somatic symptom reporting in women (see Barsky et al., 2001, for discussion). However, these explanations have not been extended to account for why women often present with worse objective interoceptive accuracy than men across a range of non-nociceptive internal signals (e.g., relating to cardiac, gastric, or respiratory state). Building on the proposal that female physiology (e.g., experiences of menstruation, lactation, pregnancy and menopause) may draw women’s attention to their bodily sensations (e.g., Barsky et al., 2001), here we advance

the proposal that atypical interoception (both heightened attention and poor interoceptive accuracy) in women may result, in part, from the dramatic physical changes women experience at several points across typical development (e.g. during adolescence, across the menstrual cycle, pregnancy, and menopause; see also Harshaw, (2015) for a discussion related to depression).

Whilst systematic investigation of the impact of physical and hormonal change on interoception has yet to be conducted, physical and hormonal change is associated with fluctuations in physical systems from which interoceptive signals arise (e.g., increased resting heart rate in pregnancy, palpitations during pregnancy, menopause and the luteal phase of the menstrual cycle; e.g., Hill & Pickinpaugh, 2008; Rosano, Rillo, Leonardo, Pappone, & Chierchia, 1997). With respect to interoception, it is possible that physical and hormonal change may result in frequent discrepancies between actual and expected bodily states (i.e., the body's current state is unexpected given the psychological or environmental context; e.g., Paulus & Stein, 2010). This in turn could contribute towards the heightened attention to internal signals and increased somatic complaints reported by women. Likewise, physical and hormonal change may also contribute towards poor objective interoceptive accuracy; 1) internal signals may be more difficult to perceive as a result of the direct effect of hormonal fluctuations on the physical systems from which interoceptive signals arise (for example, higher resting heart rate is often associated with decreased cardiac interoceptive accuracy, and pregnancy is associated with elevations in resting heart rate; e.g., Knapp-Kline, & Kline, 2005; Hill & Pickinpaugh, 2008) and 2) if, as has been proposed, interoceptive predictions are based on one's prior experiences (e.g., Barrett & Simmons, 2015), frequent discrepancies between actual and expected bodily states may also produce imprecise predictions regarding the expected state of one's body. Ultimately, if physical change renders interoceptive sensory information less reliable, this could result in a reduced propensity to use internal information.

Consistent with this notion, there is evidence that women are more likely to utilise external cues (e.g. food consumption) for gauging internal physical states (e.g. blood sugar) than men (Pennebaker and Roberts, 1992). Whilst this can result in comparable accuracy to men (Pennebaker and Roberts, 1992), the use of this indirect method means women may not benefit from the wealth of information provided by internal cues for other aspects of cognition (e.g., social cognition or emotion regulation; Khalsa et al., 2018).

If the theory that physical change disrupts interoception is correct, it follows that disrupted interoception could contribute towards mental illness *during* and *beyond* periods of physical change. This could partly explain why mental illness often manifests during periods of physical change (Altemus et al., 2014) and why women, who experience more physical change than men, are more likely to experience mental illness (Whiteford et al., 2015). *During* the period of physical change, disrupted perception and prediction of interoceptive signals may contribute to specific, temporary, psychiatric symptoms (e.g., emotional instability), cognitive irregularities, and episodic mental illness (e.g., post-natal depression). However, the impact of atypical interoception on mental health may persist *beyond* the period of physical change; typical interoceptive development is thought to depend upon the ability to learn and contextualise associations between salient interoceptive signals and external cues (Quattrocki and Friston, 2014). For example, it has been suggested that infants may learn to associate their caregivers face with interoceptive feelings of warmth and satiety which in turn may drive attachment behaviour and social attention (Quattrocki and Friston, 2014). Although this associative learning process has been proposed to be integral for development in infancy, any period in which substantial physical change occurs may require (re)learning and contextualisation of new or altered interoceptive sensations (Murphy et al., 2017). Importantly, if interoceptive sensations are volatile because of physical change, this may promote atypical learning and contextualisation of internal-external associations. In turn, this

could produce chronic interoceptive atypicalities that lead to enduring cognitive irregularities and long-term mental illness. Finally, it is also possible that the impact of interoceptive atypicalities during and beyond periods of physical change (adolescence, pregnancy and menopause) may be exacerbated by the significant social and personal changes that also occur during these life stages (e.g., Fuhrmann, Knoll & Blakemore, 2015; Laney, Hall, Anderson & Willingham, 2015; Hodgkinson, Smith, & Wittkowski, 2014; Hofmeier et al., 2017).

Above we have proposed that major physical and hormonal transitions may represent risk periods for the development of atypical interoception which in turn may increase risk of mental illness. We suggest that the different pattern of interoceptive processing observed in women, compared to men, may result from the increased amount of physical change experienced by women across development. Given links between interoception and mental health, we argue that sex differences in interoception may partly explain sex differences in the prevalence and presentation of certain mental illnesses. Further scrutiny of the impact of physical and hormonal change on interoception, and subsequently mental health, would shed light on how individual differences in interoception emerge across development and may contribute towards our understanding of sex differences in mental illness.

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